REMARKS

I. Status of the Application

This paper responds to a non-final Office action mailed June 21, 2006. The application was originally filed with claims 1-15. Following a first Office action, mailed September 13, 2004, Applicant amended claims 1-3, 5-10, and 13-15. In response to a final Office action, mailed February 28, 2005, Applicant filed an RCE which included an after final amendment that modified claim 14, canceled claim 15 without prejudice or disclaimer, and added claim 16. Following an Office action mailed June 21, 2005, Applicant amended claims 1, 2, 6, 7, 9, 10-12, 14 and 16, and added new claim 17. A final Office action mailed December 9, 2005 rejected claims 1-14, 16 and 17, and in response, Applicant filed an RCE which included an after final amendment that amended claim 16, canceled claim 17 without prejudice or disclaimer, and added new claim 18. The present paper amends claims 1, 6, 9-14, and 18, cancels claim 16, and adds new claim 19. Therefore, claims 1-14, 18, and 19 are currently under consideration in the present application. Applicant respectfully requests reconsideration of the pending claims in view of the above amendment and the following remarks. By action taken here, Applicant does not intend to surrender any range of equivalents beyond that needed to patentably distinguish the claimed invention as a whole over the prior art. Applicant expressly reserves all such equivalents that may fall in the range between Applicant's literal claim recitations and combinations taught or suggested by the prior art.

II. Amendment of Claims 1, 6, and 9-14, and Addition of New Claim 19

Applicant has amended claims 1, 6, 9, and 20 so that each claim recites "an amino acid selected from the group consisting of gabapentin and pregabalin"; has amended claims 11-13 so that each claim refers to "the amino acid" of claim 1, 9 or 10; has rewritten prior independent claims 14 and 18 so that they each depend on claim 1; and has renumbered claim 16 as new claim 19. Support for use of the identifier "amino acid" in the Markush group can be found in the specification at page 1, lines 12-13 and 18-20, and page 2, lines 15-19.

III. Objection to Claim 16 Under 37 CFR § 1.75(c)

The Office action objected to multiple-dependent claim 16 under 37 CFR § 1.75(c) for improperly depending on a higher-numbered claim. Applicant has renumbered claim 16 as claim 19, so that the latter claim refers only to claims that precede it (claims 1, 14 or 18). Applicant respectfully requests withdrawal of the objection.

IV. Rejection of claims 1-14 and 18 Under 35 U.S.C. § 103

The Office action rejected claims 1-14 and 18 under 35 U.S.C. § 103 as being unpatentable over WO 99/58573 in view of Zour et al. According to the Office action, the "'573 reference discloses solid and liquid pharmaceutical compositions comprising gabapentin analogs with increased stability" and includes "amino acids that are disclosed as agents capable of inhibiting lactam formation." The Office action notes that the '573 reference discloses "[s]weetening agents, such as mannitol and xylitol" which "may also be added to the compositions 'if needed'." The Office action further states that "Zour et al. disclose stability studies of gabapentin in aqueous solutions" which "demonstrates that the stability of gabapentin in aqueous solution is greatest at a pH of 6.0, and at 45 °C gabapentin demonstrated minimal degradation when formulated at a pH from 5.5 to 7.0." Applicant respectfully submits that claims 1-14, 18 and 19 are patentable over WO 99/59573 and Zour et al.

Applicant submits that the combination of WO 99/58573 and Zour et al. do not render the claims *prima facie* obvious, because modifying the '573 reference as suggested by the Office action would change the principle of operation of the reference. *See* MPEP § 2143.01(VI) (8th ed., Rev. 5) ("If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious."). As noted in the application, Applicant has discovered that gabapentin or pregabalin can be formulated in a stable liquid pharmaceutical composition having low levels of lactam when the pH of the composition is about 5.5 to about 7.0 and when the composition includes one or more polyhydric alcohols. See Specification, page 4, lines 4-

7, and page 9, lines 7-9. Moreover, the stable formulation is achieved without the inclusion of an additional amino acid, such as glycine. *See, e.g.*, claims 1, 6, 9 and 10, above. As noted in the Office action, WO 99/59573 requires the presence of an additional amino acid to inhibit lactam formation, and therefore its absence would change the principle of operation of the reference.

Furthermore, Applicant submits that WO 99/59573 teaches away from inclusion of a polyhydric alcohol in pharmaceutical compositions containing gabapentin or pregabalin without concomitant use of an additional amino acid to stabilize the formulation. For instance, Example 2 in WO 99/59573 shows that the addition of a polyhydric alcohol (xylitol, sample "e") to an aqueous gabapentin solution increases lactam formation (compare sample "d" and sample "e" in Table 4). In contrast, the addition of glycine (sample "f") to an aqueous solution of gabapentin and xylitol decreases lactam formation (compare sample "f" with samples "d" and "e" in Table 4). The Office action contends that WO 99/59573 does not teach away from the claimed invention because "the 'comprising' language of the present claims allows for the presence of both xylitol and glycine." As noted above, however, Applicant has amended the claims so that they exclude any amino acid (e.g., glycine) that would prevent lactam formation.

Applicant further submits that the claimed pH range and the use of one or more polyhydric alcohols in the claimed amounts result in pharmaceutical compositions having surprising and unexpected chemical stability. To support this conclusion, Applicant submitted in its response of April 7, 2006, a declaration under 37 CFR § 1.132, which described data that showed the influence of pH and the presence of a polyhydric alcohol on lactam formation. The data indicated that aqueous compositions containing gabapentin exhibited improved stability when formulated at a pH of about 5.5 to about 7.0, and that aqueous gabapentin formulations containing a polyhydric alcohol generally exhibited improved stability over formulations that did not. *See* Applicant's Response of April 7, 2006 at pages 7-8 and Declaration Under 37 CFR § 1.132.

Finally, Applicant submits that the stability of the claimed formulations in the absence of an amino acid besides gabapentin or pregabalin is itself an indicia of unobviousness. *See* MPEP § 2144.04(II.B) (8th ed., Rev. 5) ("Omission of an element with retention of the element's function is an indicia of unobviousness."). In view of the above, Applicant submits that the pending claims are patentable over WO 99/58573 and Zour et al., and respectfully request withdrawal of the rejection.

V. Conclusion

In view of the foregoing, Applicant respectfully submits that all pending claims are patentable over the prior art of record. If the Examiner has any questions, Applicant requests that the Examiner telephone the undersigned.

Applicant submits that no fees are due in connection with the filing of this paper. However, if Applicant has overlooked any required fees, please charge the fees to deposit account number 23-0455.

Respectfully submitted,

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